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Comparison of depression and anxiety in inflammatory bowel patients treated with anti-TNF or immune modulators

Esra ÇATALTEPE[1], Nergiz EKMEN[2,*], Mehmet CİNDORUK[2]

[1]Department of Geriatrics, Faculty of Medicine, Gazi University, Ankara, Türkiye
[2]Department of Gastroenterology, Faculty of Medicine, Gazi University, Ankara, Türkiye

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Abstract

The aim of this study was to investigate patients diagnosed with inflammatory bowel disease (IBD), the effects of drug groups used in the treatment of inflammatory bowel disease on depression and anxiety. This study was a single-center prospective study involving 94 patients with inflammatory bowel disease, 51 of whom had ulcerative colitis (UC) and 43 had Crohn's disease (CD). Harvey-Bradshaw activity scores for CD and Mayo Clinic activation scores for UC were calculated. Depression and anxiety data were collected with the Beck Depression Inventory and Beck Anxiety Inventory. The mean age for UC and CD were 40.25 ± 14 and 38.9 ± 13.8 years, respectively. There was a positive correlation between disease activation and depression and anxiety levels in both IBD subgroups ($p<0.05$). All patients included in the study were compared in terms of depression and anxiety levels before and after treatment, and a statistically significant improvement was found with the remission of both ulcerative colitis and Crohn's disease ($p<0.001$). There was a significant difference in depression and anxiety levels before and after treatment according to treatment options ($p<0.001$). There is a positive relationship between the disease activation score and the level of depression and anxiety in IBD. Immunosuppressive and immunomodulatory drugs used in the treatment of IBD may also improve the parameters of depression and anxiety in this disease.

Keywords: ulcerative colitis, Crohn disease, depression, anxiety, disease activation

1. Introduction

Both Crohn's disease (CD) and ulcerative colitis (UC) are chronic inflammatory diseases that affect the gastrointestinal system. They impair quality of life and are characterized by periods of relapse and remission. In the general population, the prevalence of depression and anxiety is higher in patients with chronic diseases (1).

Studies have shown that the frequency of depression and anxiety is higher in patients with inflammatory bowel disease (IBD) compared to the general population (2). While depressive symptoms can affect the activity of the disease, higher rates of depression and anxiety have been reported in the active phase of the disease compared to the remission period. Anxiety and depression rates are between 29-35% in the remission period; at the time of relapse, this rate goes up to 80% for anxiety and 60% for depression (2).

Improvement in IBD activity has also been linked to a reduction in the severity of depressive and anxiety symptoms, according to research. Several studies suggest that anti-tumor necrosis factor alpha (anti-TNF), an agent used in the treatment of IBD, may reduce depressive symptoms and improve quality of life. In addition, there are data showing that immunomodulatory treatment types such as azathioprine and methotrexate, which are widely used in the treatment of IBD, also benefit depressive symptoms.

In this study, it was aimed to evaluate the effect of any newly initiated immunosuppressive therapy (anti-TNF therapy or immunomodulatory therapy) on anxiety and depression symptoms in the active phase of inflammatory bowel disease. We aimed to evaluate whether the regression in disease activity is associated with improvement in depressive symptoms and whether it differs in the level of depression according to the treatment options they receive.

2. Materials and methods

2.1. Study design

This study was conducted between June 2018 and January 2019. Patients with active UC and CD who applied to the gastroenterology outpatient clinic or followed up in the gastroenterology service were included. Depression and anxiety data of the patients were obtained with the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI), and the relationship between the treatment they received and depression and anxiety were evaluated.

*Correspondence: dr_nergisekmen@hotmail.com

The patients were informed about the study, and a written consent form was obtained from the patients before starting the study.

Inclusion Criteria

- To be diagnosed with IBD clinically, endoscopically and pathologically
- Being in active disease

Exclusion Criteria

- Refusing to volunteer and sign the consent form
- The inability to read or write.
- Presence of substance abuse, psychiatric illness or any neurological disease
- Using psychotropic medication in the last 1 year

Workflow

After clinical, laboratory, endoscopic and histological evaluation, patients diagnosed with active IBD according to the current ECCO guideline and followed up in the Gastroenterology outpatient clinic and service were asked whether they would like to be included in the study. The study was explained in detail to the patients who stated that they wanted to participate, and their written consent was obtained. All patient groups were evaluated twice with the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) before starting treatment and 3 months after starting inflammatory bowel disease treatment. The questionnaires were filled by the person participating in the study after being informed by the doctor. Before starting treatment, disease activity on the day of the survey was semi-quantitatively determined and recorded by the Harvey-Bradshaw Index for CD and Mayo scoring for UC. Whether the patients were in remission or not was determined according to these indices.

2.2. Data collection tools

Beck Depression Scale

It is used to have information about the risk of depression and to measure the level and severity of depressive symptoms. It was developed by Beck et al. The Turkish validity and reliability study of the BDI was conducted (3). It is a self-evaluation scale. It can be applied to both healthy individuals and psychiatric patients. It consists of a total of 21 self-evaluation sentences. Each question is evaluated on a scale of 0 to 3. It ranges from 0 to 63 in total and is classified as follows; (4).

- Normal 0-9
- Mild depression 10-18
- Moderate depression 19-29
- Severe depression 30-63

Beck Anxiety Scale

It is an inventory consisting of 21 questions developed by Beck et al (5). Each question is evaluated between 0 and 3 and categorized as follows;

- Minimum anxiety 0-7
- Mild anxiety 8-15
- Moderate anxiety 16-25
- Severe anxiety 26-63

Mayo Clinic Ulcerative Colitis Disease Activity Index

It is a scoring system that grades the severity of the disease in the follow-up of UC. Results are obtained by evaluating stool pattern, rectal bleeding severity, endoscopic findings and general well-being of the physician.

It ranges from 0 to 12 in total and there is a positive correlation between the increasing score and the severity of the anxiety clinic/disorder. Score of 2 points or less is associated with remission, 3-5 points mild disease, 6-10 points moderate disease, and 11-12 points severe disease.

Harvey-Bradshaw Index

It is used to evaluate the severity of the disease in the follow-up of CD. Scoring is done by stool pattern, mean number of abdominal pains, general well-being, systemic complications, and whether there is a mass in the abdomen. A score of less than 5 is associated with remission, a score of 5-7 is associated with mild disease, a score of 8-16 is associated with moderate disease, and a score greater than 16 is associated with severe disease.

2.3. Statistical analysis

Data analysis was performed using the Statistical Package for the Social Sciences 22 (SPSS, Inc, Chicago IL, USA). As a statistical analysis, in the descriptive findings section, categorical variables will be presented as numbers and percentages, and continuous variables will be presented as mean±standard deviation for normally distributed data and median (min, max) for non-normally distributed data, and number of cases and (%) for nominal variables. The Mann-Whitney U-test was used to compare categorical data between groups that did not show a normal distribution. The Wilcoxon test was used to compare the continuous data between groups after checking whether they fit the normal distribution. The p value < 0.05 was accepted as significant according to the 95% confidence interval.

3. Results

127 patients, including 73 UC and 54 CD, were evaluated for the study, 9 of these patients did not come for follow-up after 3 months, and 24 patients were excluded because they had one or more of the exclusion criteria. Thus, a total of 94 patients were included (39.65 ± 13.93 years), 51 patients with UC (21 female), 43 patients with CD (23 female). In the mean age was 40.25±14 in UC and 38.9±13.8 in CD. There was no significant difference between the groups in terms of age and gender.

3.1. Disease activity

The mean of Harvey-Bradshaw Index, which was an activation indicator for CD, was 8.09 ±1.9, while the lowest activity score

was 5 and the highest was 13. According to the Harvey-Bradshaw index, 46% of patients with CD had a mild disease and 53.5% had a moderate disease. For UC, the mean of Mayo Clinic UC activity index was 7.75 ±1.32 and while the lowest activity score was 4 and the highest was 11. According to the Mayo Clinic UC activity index, 9.8% of UC patients had a mild disease, 86.3% had a moderate disease, and 3.9% had severe disease.

3.2. Beck Depression Inventory and Beck Anxiety Inventory Scores

BDS ranged from 0 to 23, and the mean was 14.72±5.07 in the entire patient group before treatment. It was determined that 12.8% of the patients were normal, 63.8% mild depression, 22.3% moderate depression and 1.1% severe depression before treatment.

BAS ranged from 0 to 28, and it was 10.29±3.68 in the entire patient group before treatment. It was found that before the treatment, 23.4% of the patients had minimal anxiety, 64.9% had mild anxiety and 11.7% had moderate anxiety.

The mean BDS was 13.89±4.98 in females and 15±5.09 in males in the entire patient group before treatment. Before treatment, the mean BAS was 10±3.48 in women and 10.5±3.8 in men. There was no significant difference in depression and anxiety levels according to gender before and after treatment. (p>0.05).

It was determined that there was a change in this mean, as 5.88 ± 2.20 for BDS and 3.27 ± 2.02 for BAS, 3 months after starting IBD treatment. Similarly, a statistically significant difference was found in UC patients in terms of depression and anxiety levels before and after treatment (p<0.001) (see Table 1).

In patients with CD, the mean BDS was 15.6±5.38 and the BAS was 11±3.74 before treatment. It was detected that 3 months after starting the inflammatory bowel disease treatment, the mean BDS changed to 6.33±2.27 and the mean BAS was 3.56±2.42.

It was observed that there was a statistically significant difference between depression and anxiety levels before and after treatment in CD patients, as in patients with UC. (p<0.001) (see Table 1).

There was a significant decrease in anxiety and depression scores before and after treatment in anti-TNF and anti-integrin, 5-ASA, 5-ASA±azathioprine treatment groups (p<0.001) (see Table 2).

Table 1. Comparison of depression and anxiety levels before and after treatment in the study population

	Before treatment BDS	After treatment BDS	*p*	Before treatment BAS	After treatment BAS	*p*
CD	15,6±5,38	6,33±2,27	<0,001	11±3,74	3,56±2,42	<0,001
UC	13,96±4.97	5,88±2,20	<0,001	9,69±3,56	3,27±2,02	<0,001

Wilcoxon Test was used. UC, ulcerative colitis; CD, Crohn's disease; BDS, Beck depression scale; BAS, Beck anxiety scale

Table 2. Change in anxiety and depression levels in the study group according to the treatment they received

	Before BDS	After BDS	*p*	Before BAS	After BAS	*p*
5-ASA n=24	11.29±4.80	5±2.24	<0,001	9.04±3.82	2.58±1.99	<0,001
Azathioprine n=21	13.43±4.74	5.52±1.7	<0,001	9.38±2.71	2.86±1.79	<0,001
Anti-TNF and anti-integrin n=49	16.96±4.40	6.86±2.15	<0,001	11.29±3.75	4.04±2.30	<0,001

Wilcoxon Test was used. UC, ulcerative colitis; CD, Crohn's disease; BDS, Beck depression scale; BAS, Beck anxiety scale

A positive correlation was assigned between the level of disease activation and depression and anxiety in both UC and CD patients (see Table 3)

Table 3. Evaluation of the relationship between activation scores and Beck depression and anxiety scores in the study group

	Beck Depression score		Beck Anxiety Score	
	r	*p*	*r*	*p*
Mayo score, n=51	0.780	<0.001	0.474	0.001
Harwey-Bradshaw, n=43	0.708	<0.001	0.474	0.001

r: Spearman's Correlations Coefficient

4. Discussion

Although psychiatric diseases are a public health problem that negatively affects general health, the presence of chronic diseases is one of the stressor factors that facilitate the emergence of psychiatric diseases such as anxiety and depression or negatively affect the prognosis.

Recent studies have noted increased rates of depression and anxiety in patients with IBD (6). In studies on IBD and other chronic diseases, the prevalence of depression was found to be 6-14% (1, 7). In our study, the prevalence of depression at baseline was higher than in other studies. This can be explained by the inclusion of patients in the active disease stage in the study.

Likewise, the presence of anxiety and depression negatively affects the prognosis of chronic diseases. A prospective study reported that individuals with IBD who had higher depressive symptoms at disease onset were more likely to relapse than individuals without depression. (8).

Studies show that IBD treatment can actually affect depressive symptoms. Minderhoud et al. found a significant improvement in depressive symptoms after one or two infusions of infliximab every 14 weeks with CD (9). Similar to the previous study, improvement in depressive symptoms was observed in a small study of 15 patients who received a single infliximab infusion and were followed for 8 weeks (10). Similarly, in our study, we found a significant decrease in the number of patients with moderate and severe depression symptoms in the 3-month follow-up after starting IBD treatment.

Some small studies have found that improvement in depressive symptoms in inflammatory diseases such as CD and ankylosing spondylitis is not associated with improvement in disease activity after anti-TNF therapy (10, 11). In our study, on the contrary, significant improvement in depression and anxiety symptoms was observed in both groups receiving anti-TNF therapy and immunomodulatory therapy.

Improvement of depressive symptoms may not be due to the initiation of IBD treatment alone. On the contrary, there is important literature that also associates depression with the proinflammatory process and disease activation (12). Supporting this association, a randomized placebo-controlled trial evaluated the role of infliximab in the treatment of patients with treatment-resistant depression independent of inflammatory disease. They found no significant improvement in depressive symptoms with infliximab treatment, but improvement in depressive symptoms was found in patients with high baseline C-reactive protein (CRP) levels (hCRP>5 mg/l) (13). In the current study, high depression and anxiety scores in the active period may be associated with high CRP and active pro inflammatory processThere is a positive correlation between the decrease in CRP level after the patients enter remission and the decrease in depression and anxiety symptoms.

In the present study, depression and anxiety levels in the active disease period were found to be significantly higher than in the remission period, similar to other studies. A decrease in depression and anxiety levels may be due not only to the decrease in disease activity, but also to the improvement of multifactorial causes such as discontinuation of corticosteroids used in the active period, improvement of other medical conditions or the passage of time.

The small number of patients, lack of sociodemographic data, previous use of corticosteroids, smoking status and incomplete data on sociocultural status are the weaknesses of our study. These incomplete data make it difficult to control for confounding factors affecting depression and anxiety symptoms.

The Beck depression and anxiety questionnaire was approved for the assessment of depressive symptoms. However, it is not a definitive method to evaluate depressive disorders. Another factor limiting our study is that the depression status of the patients could only be obtained with Beck depression and anxiety scores in a short time during hospital visits.

In conclusion, the present study highlights the importance of treating all aspects of the disease, including psychological comorbidities such as depression, in patients with IBD. At the same time, it should be kept in mind that depressive and anxious symptoms may accompany the disease and even adversely affect the prognosis of the disease.

This study shows that; immunosuppressive and immunomodulatory drugs that make IBD go into remission can also improve psychological parameters in this disease.

More research is needed in this area to understand both the pathophysiology of IBD and the most common psychological comorbidities associated with the disease.

Ethical statement

The study was designed as a prospective study approved by the ethics committee of Gazi University Faculty of Medicine, Ankara, Turkey (Approval number: 254-2018/05, Date: 05.06.2018). The study protocol was designed in accordance with the ethical guidelines of the Declaration of Helsinki published in 1975.

Conflict of interest

The authors have no conflicts of interest to declare.

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None to declare.

Authors' contributions

Concept: E.Ç., N.E., M.C., Design: E.Ç., N.E., M.C., Data Collection or Processing: E.Ç., N.E., M.C., Analysis or Interpretation: E.Ç., N.E., M.C., Literature Search: E.Ç., N.E., M.C., Writing: E.Ç., N.E., M.C.

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